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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/310,685	05/04/99	LAMB J	674525-2001

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EXAMINER	
VANDER VEGT, F	
ART UNIT	**PAPER NUMBER**
1644	10

DATE MAILED: 01/16/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/310,685	Lamb et al
Examiner	**Group Art Unit**
F. Pierre VanderVegt	1644

☒ Responsive to communication(s) filed on *Nov 2, 2000*.

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), ~~or thirty days, whichever is longer~~, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-32* ~~is~~/are pending in the application.

Of the above, claim(s) *1-12, 18-25, and 27-32* ~~is~~/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *13-17 and 26* ~~is~~/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

This application is a continuation-in-part of application serial number PCT/GB97/03058.

New claims 27-32 have been added.

Claims 1-32 are currently pending in this application.

Election/Restriction

1. Applicant's election of Group I, claims 1-6, 13-17 and 26, in Paper No. 9, filed November 2, 2000, is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election **without traverse** (MPEP § 818.03(a)).

Claims 1-6 have been amended to recite a method of using *Notch*-ligand for immunotherapy. The claims are now drawn to a method which is distinct from the elected invention of a *Notch* ligand compound. Accordingly, these claims are not being examined in the present Office Action.

New claims 27-32 have been added by the amendment filed November 2, 2000 and are drawn to methods distinct from the elected invention of a *Notch* ligand compound. Accordingly, these claims are not being examined in the present Office Action.

2. Claims 1-12, 18-25 and 27-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions. Election was made **without** traverse in Paper No. 9.

Accordingly, claims 13-17 and 26 are the subject of examination in this Office Action.

Claim Rejections - 35 USC § 112

3. Claims 14 and 16 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *Notch* ligands, including Serrate and Delta family members, does not reasonably provide enablement for derivatives or analogs of *Notch* ligands or *Notch* as a *Notch* ligand. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly as claimed in claims 14 and 16 without an undue amount of experimentation. The scope of claim 14 is not commensurate with the enablement provided by the disclosure with regard to *Notch* ligand derivatives and analogs. Since the amino acid sequence of a peptide determines its structural, immunogenic and functional properties, predictability of which changes can be tolerated in a derivative of the peptide's amino acid sequence and still retain similar functionality requires a knowledge of and guidance with regard to which amino acids in the peptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which a protein's structure relates to its immunogenic determinants and functional usefulness. However, the problem of predicting peptide structure and what changes can be tolerated with respect thereto is complex and well outside the realm of routine experimentation. Further, the recitation of analogs, encompassing "peptidomimetics" does not find enabling support in the instant specification because peptidomimetics are not protein sequences and the prediction and knowledge of non-peptide structures which can effectively mimic the structure and function of a peptide falls well beyond the realm of routine experimentation. The scope of claim 16 is not commensurate with the enablement provided by the disclosure with regard to derivatives of *Notch* which can bind to and modulate the activity of *Notch* protein. No such *Notch* derivatives have been disclosed, nor has a method for screening or isolating them. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute.

4. Claims 3-17 and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth *Notch* ligands of the *Serrate* and *Delta* families and therefore the written description is not commensurate in scope with the claims drawn to any "derivatives or analogs thereof" [claim 14] or a derivative of "*Notch*" [claim 16].

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111), clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). It is respectfully submitted that the instant specification, in fact, states at page 12, lines 11-16 that said "derivatives" and at page 12, line 25 to page 13, line 3 that said "analogs" were not in Applicant's possession as of the filing date sought. The passages refer to types of putative peptides or peptidomimetics which may modulate *Notch-Notch* ligand interactions but do not provide even a single example of such a molecule. In addition, the recitation of *Notch* derivatives in claim 16 does not find written support in the instant specification as there is no evidence provided that Notch is capable of binding to itself.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115).

With the exception of *Notch* ligands of the *Serrate* and *Delta* families, the skilled artisan cannot envision the detailed structure of the encompassed proteins and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The protein itself is required. See *Fiers v. Revel*, ((CAFC, 1993) 25 USPQ 2d 1601) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*,((CAFC, 1991) 18 USPQ2d 1016).

Furthermore, In *The Reagents of the University of California v. Eli Lilly* ((CAFC, 1997) 43 USPQ2d 1398), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention." It is respectfully submitted that the facts in the instant application, while drawn to proteins, read upon the situation in *U of C v. Lilly,* drawn to nucleic acids, because the instant specification does not recite a representative number of proteins, defined by an amino acid sequence, in order to define what falls within the scope of the claimed genus of *"Notch* ligand derivatives or analogs" or of *Notch* derivatives which bind to *Notch* to convey to the artisan that such derivatives or variants were in Applicant's possession at the time of filing. No disclosure beyond the mere mention of derivatives or analogs is made in the specification. This is insufficient to support the recitation in the claims of "derivatives or analogs" as provided by the Written Description Guidelines published in the January 5, 2001 Federal Register at Volume 66, Number 4, pages 1099-1111.

5. Claim 26 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 26 provides for the use of *Notch* ligand, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process Applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claim 26 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 26 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Artavanis-Tsakonas et al (AJ on form PTO-1449).

The Artavanis-Tsakonas et al reference teaches *Notch* ligands and the use of those ligands to modulate the signaling of *Notch*. The prior art teaching clearly anticipates the claimed invention.

Conclusion

8. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

9. Papers related to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in

the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for official documents to be entered into the record for Art Unit 1644 is (703)305-3014.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to F. Pierre VanderVegt, whose telephone number is (703)305-6997. The Examiner can normally be reached Tuesday through Friday and odd-numbered Mondays (on year 2000 366-day calender) from 6:30 am to 4:00 pm ET. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ms. Christina Chan can be reached at (703)308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist, whose telephone number is (703)308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
Technology Center 1600
January 11, 2001

F. PIERRE VANDERVEGT
PATENT EXAMINER